

Joint Trust Guideline for the Use of β -blockers in the Management of Capillary Haemangiomas in infancy

A clinical guideline recommended for use

For Use in:	NICU and Paediatric Outpatients
By:	Medical and Nursing staff
For:	Infants with rapidly expanding capillary haemangiomas which pose a threat to life or vital organ function
Division responsible for document:	Women and Children's Services
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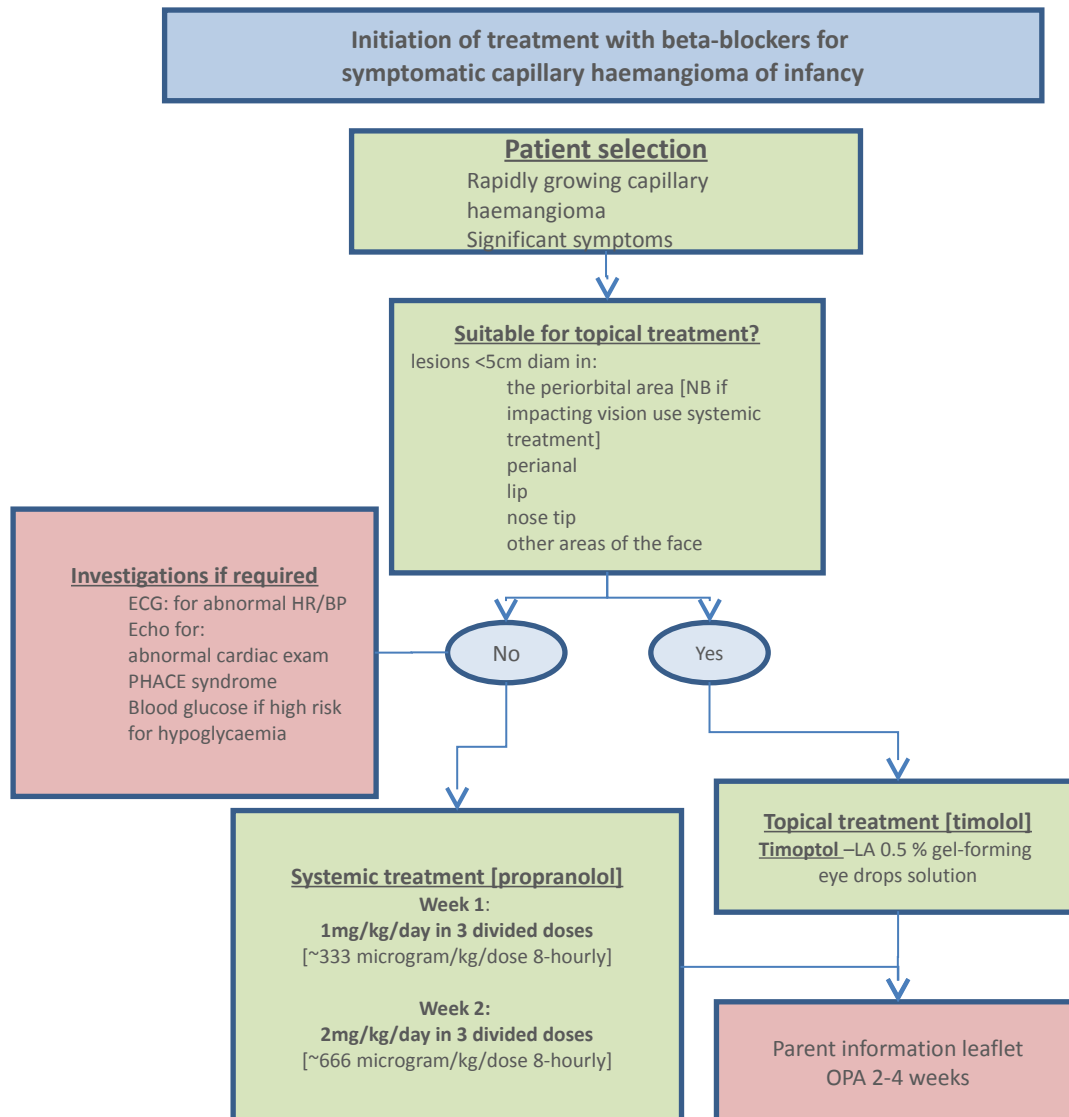
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JCG0084v1	27/06/2014	Change of header and footer to joint hospital version. JPUH changed to ward names and reference to CA4093 Pg4 in their version.	Mark Dyke
3.1	19/01/2022	No clinical changes. Leaflets loaded as separate documents.	Mark Dyke

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Quick reference guideline/s



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1. Objective

To guide the selection of patients with rapidly expanding capillary haemangiomas (strawberry naevi) for treatment with β -blockers, either systemically [propranolol] or topically [timolol]. To offer guidance to the pre-treatment assessment, dosage schedule and monitoring required to facilitate safe initiation of such treatment.

2. Rationale

Capillary haemangiomas come in several forms but the commonest, the “strawberry haemangioma” affects up to 10% of infants. Its natural history is one of onset within a few weeks after birth, a phase of rapid growth over several months (usually completed within the first 6-8 months), followed by spontaneous involution over a period which may last from a few months to several years. The vast majority are benign, causing few if any symptoms beyond the, sometimes distressing, cosmetic effects. Once involution is finished, the resolution is usually complete with a good cosmetic result although, particularly in the case of some bulkier lesions, a patch of skin may be left which is pale or atrophic. The appearance of large areas of loose skin may subsequently be improved surgically.

Exceptionally, the rapid growth of a lesion may cause significant morbidity (such as the loss of sight from an eye where a large lesion of the eyelid prevents eye opening) or even life-threatening complications (e.g. where a lesion threatens the nasal or tracheal airway). In these circumstances, treatment may be needed urgently. In the past, treatment options were limited to pulsed-dye laser or drug treatment with high-dose systemic steroids or interferon with very significant risks of serious side effects. Since 2008, when the first case report was published of a serendipitous response of a large haemangioma to the use of Propranolol, many publications have described successful treatment with Propranolol as sole treatment for this condition. Although side effects are described, published accounts of serious adverse effects are very few and, on balance, the risk-benefit profile seems favourable to alternative strategies. More recently, similar benefits have been described for smaller lesions using topical timolol.

3. Broad recommendations for systemic treatment [Propranolol]

3.1 Patient selection: Patients should be considered for the use of Propranolol treatment if they meet all of the following criteria:

- a capillary haemangioma of the strawberry haemangioma-type which is undergoing a phase of significant growth
- a lesion which is either causing, or is considered to be at significant risk of causing, symptoms which:
 - pose a risk to the patient’s life (e.g. airway or breathing difficulties)
 - pose a risk to the health of vital organs (e.g. spinal cord, liver or eye)
 - are distressing e.g. causing pain, ulceration or bleeding

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- the patient has no contraindications to the use of Propranolol such as:
 - heart failure)
 - AV-block or other causes of bradycardia) refer to Cardiologist
 - hypotension)
 - metabolic acidosis
 - bronchospasm
 - hypoglycaemia

3.2 Protocol for initiation of treatment

Treatment may be commenced from the out-patient clinic (OPC) either at the time of the consultation [if parents have had sufficient opportunity to consider and consent] or later if parents prefer. Prior to starting systemic treatment with Propranolol, a thorough history and physical examination should be conducted in OPC.

3.3 Baseline observations and investigations

For most otherwise healthy infants no pre-treatment investigations are required.

Exceptions are:

- **ECG** if baseline HR and/or BP are outside normal range
- **Echocardiogram** for:
 - Cardiac abnormalities on examination eg murmur
 - features of PHACE syndrome which are:
 - **Posterior fossa brain malformations** present at birth
 - **Haemangioma** covering a large area on the head or neck (greater than 5 cm).
 - **Arterial lesions** [specifically abnormalities of the blood vessels in the neck or head]
 - **Cardiac abnormalities**
 - **Eye abnormalities** [including optic nerve hypoplasia, hypertrophic primary vitreous and others]
- **Baseline glucose** if the infant:
 - *is preterm and/or small for dates*
 - *is feeding poorly*
 - *has a history of hypoglycaemic episodes.*
- **MRI/MRA imaging** if features of regional syndromes are present:
 - PHACE [see above]
 - LUMBAR

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- large >5cm segmental haemangioma over perineum, gluteal cleft or lumbo-sacral
- greater than average risk of ulceration
- small risk of undergrowth/overgrowth of affected limb

3.4 Starting dose: A preparation of 1mg/ml solution is preferable

Week 1: Propranolol 1mg/kg/day in 3 divided doses
[equivalent to ~333 microgram/kg/dose 8-hourly]

Week 2: Propranolol 2mg/kg/day in 3 divided doses
[equivalent to ~666 microgram/kg/dose 8-hourly]

Medication should be given with or shortly after food. If an inter-current illness causes significant vomiting, propranolol should be temporarily withheld to reduce the likelihood of hypoglycaemia.

3.5 Dose escalation: If response is unsatisfactory after 4 weeks (and no adverse effects have occurred) the dose may be increased to:

Propranolol 3mg/kg/day in 3 divided doses
[equivalent to 1000 microgram/kg/dose 8-hourly]

3.6 Parent information: Parents should be given an information leaflet [Appendix 1] and offered advice on potential side effects:

- Bradycardia
- Heart failure
- Hypotension
- Cardiac conduction disorder
- Bronchospasm
- Peripheral vasoconstriction
- Weakness and fatigue
- Sleep disturbance
- Hypoglycaemia

3.7 Follow-up OPA: should be arranged 2-4 weeks after treatment commences

4. Recommendations for topical treatment [Timolol]

4.1 Patient selection

The use of topical timolol treatment should be considered for lesions <5cm diameter in the following locations:

- the periorbital area [NB only lesions without adverse impact on vision]
- perianal
- lip

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- nose tip
- other areas of the face

4.2 Preparation

Timoptol –LA 0.5 % timolol (as maleate) w/v gel-forming eye drops solution

4.3 Dosage and administration

The off-label use of the medication should be explained to the parents and information leaflet provided [Appendix 2]. Advice on potential side effects should be explained to parents prior to starting therapy [see section 3.6] though these are far less likely with topical therapy.

The parents should be instructed to:

- wash their hands before and after administration of timolol
- apply timolol gel one drop 1-3 times a day to the haemangioma surface and to spread the gel carefully with a finger tip over the lesion but avoiding surrounding skin
- leave the treated lesion exposed to air for up to 1 minute after application to allow gel formation

If continued growth of the lesion occurs and significant symptoms develop [eg adverse impact on vision/breathing] then systemic β -blocker treatment should be commenced.

4.4 Follow-up OPA: should be arranged 2-4 weeks after treatment commences

5. Summary of development and consultation process undertaken before registration and dissemination

This guideline was initially drafted by Dr Dyke on behalf of the Paediatric and Dermatology Departments. It was circulated for comments to Ros Howe (Paediatric Pharmacist), Neonatal and Paediatric Consultants and Drs Levell & Millington. Comments and suggested amendments were incorporated in the revised draft presented and agreed at a Departmental Guideline meeting [15.12.10]. An additional literature review in December 2015 led to a further draft, with minor modifications, which was circulated for comment to Dermatology, Paediatric and Plastic Surgery colleagues. Further minor amendments based on comments received were incorporated into a final draft submitted for approval in January 2016. Following publications on the use of topical therapy, a further modification was added in 2018 and in 2022 minor updates were added following publication of an AAP Clinical Practice Guideline

6. Clinical Audit Standards

1. All infants treated with propranolol for capillary haemangioma should meet patient selection criteria outlined in section 3.1

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2. All infants treated with propranolol for capillary haemangioma should have documented evidence of pre-treatment assessment
3. All infants treated with propranolol for capillary haemangioma should receive propranolol at the dosage schedule outlined in sections 3.4 and 3.5. Any variations from the schedule (e.g. for side effects) should be accompanied by a clear rationale in the patient notes

Distribution list/ dissemination method

- a. Hospital intranet

References/ source documents

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12. Topical Timolol for Infantile Hemangiomas: Evidence for Efficacy and Degree of Systemic Absorption [Pediatr Dermatol. Weibel L et al 2016 Mar-Apr;33\(2\):184-90. doi: 10.1111/pde.12767. Epub 2016 Feb 3.](#)
13. Oral propranolol in the treatment of proliferating infantile haemangiomas: British Society of Paediatric Dermatology Consensus Guideline. Solman L et al. British Journal of Dermatology 2018 (179); 582-589
14. Clinical Practice Guideline for the Management of Infantile Haemangiomas Krowchuk DP for the AAP Paediatrics 2019 (143):e20183475

Appendix 1

Use of Propranolol for Capillary Haemangioma of Infancy
[Trustdocs Id: 19476](#)

Appendix 2

Use of Topical Timolol for the Treatment of Small Capillary Haemangioma
[Trustdocs Id: 19477](#)